

# ROLE OF IMMUNOTHERAPY IN CANCER TREATMENT



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# Objectives



- Basics of Human Immune System



- Introduction to Immuno-Oncology



- Historical background & features of Immunotherapy



- Approaches to Cancer Immunotherapy



- Immune related Adverse Events



- Nurse's role in Cancer Immunotherapy

# Introduction

- The principal function of the immune system is to **prevent and eradicate pathogens/ infections**.
- The immune system has a **critical role in controlling cancer** through a dynamic relationship with tumour cells
- Attempts to treat different types of cancers by **stimulating immune responses to attack cancer cells** have been tried for more than a century, but only recently has immunotherapy regained clinical attention, with approvals of multiple agents for the treatment of cancer

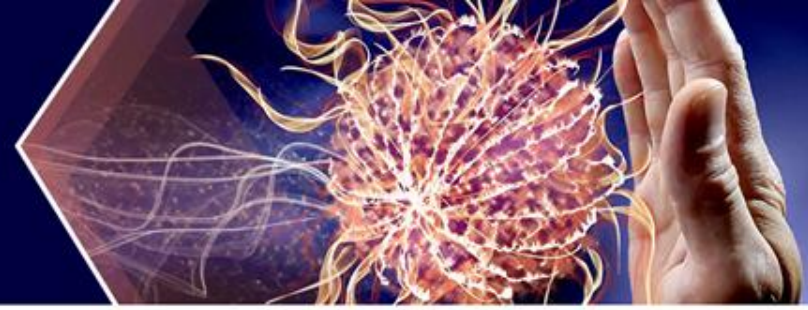


# 1. BASICS OF THE HUMAN IMMUNE SYSTEM





# Human Immune System



The immune system is a complex network that works together to defend the body against pathogens and cancer cells

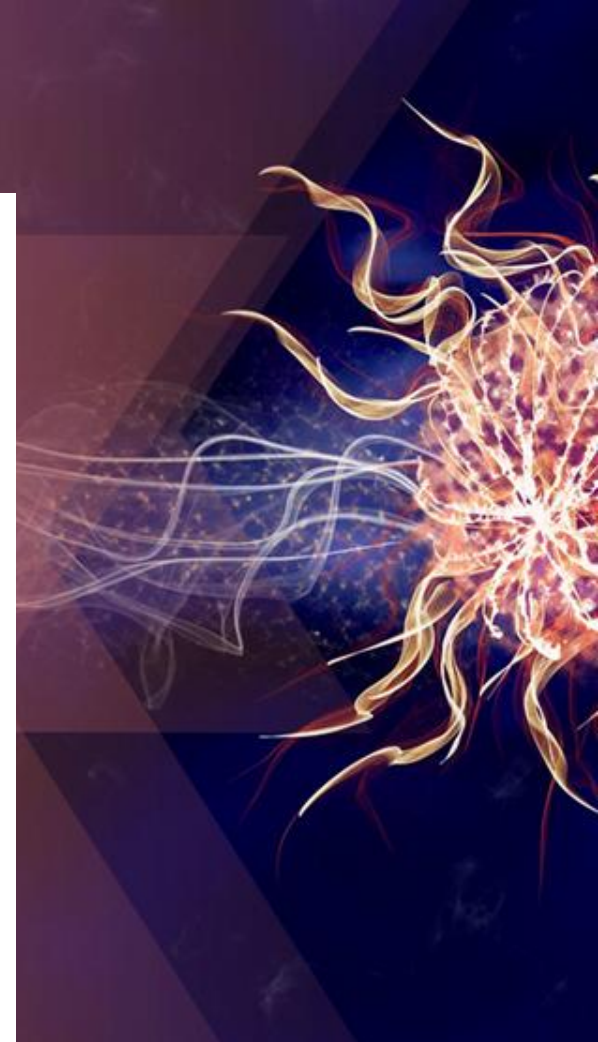
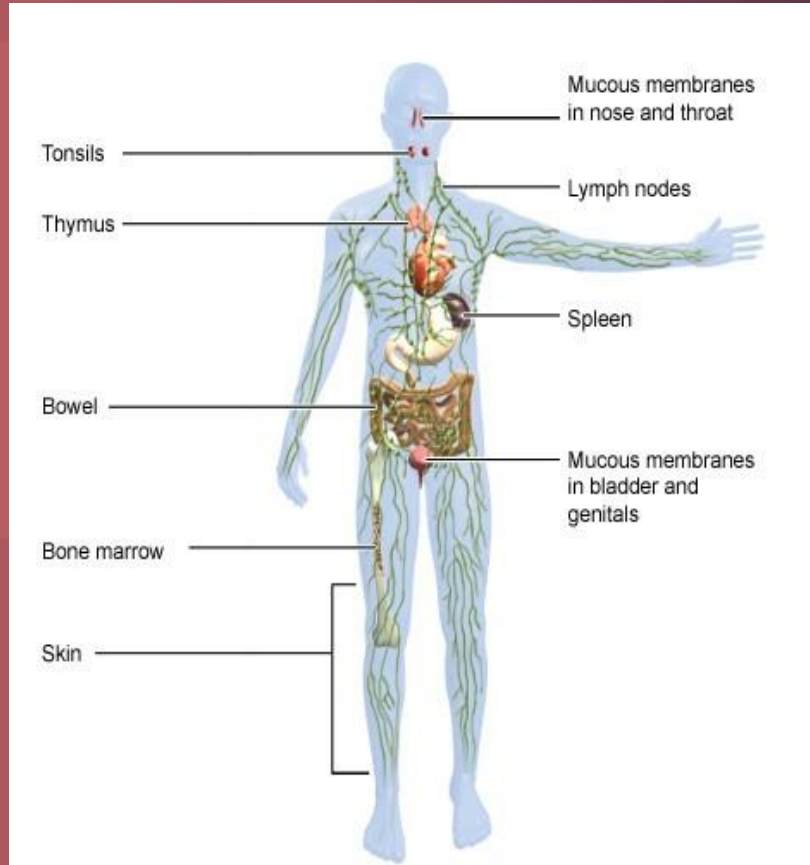
## Key Functions

- Monitors tissue homeostasis
- Protects against invading or infectious pathogens
- Removes damaged or malignant cells

## Comprises of

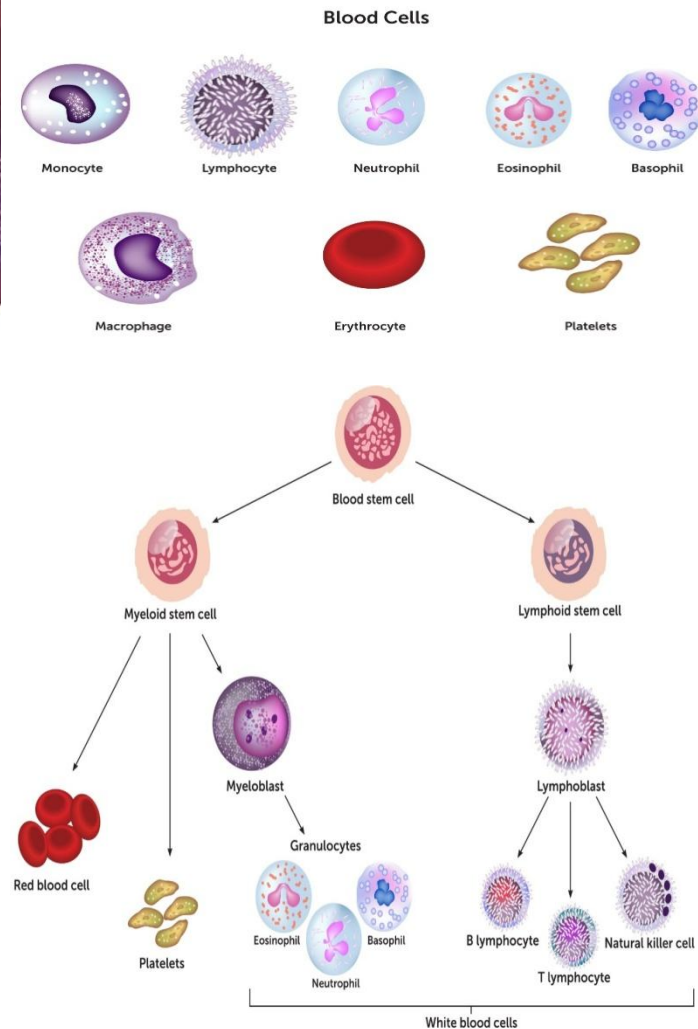
- Central , peripheral organs, tissues and cells:
- Lymphatic system, Bone marrow , Spleen , Thymus, Cutaneous / Mucosal elements

# Human Immune System



# Central organ: Bone Marrow

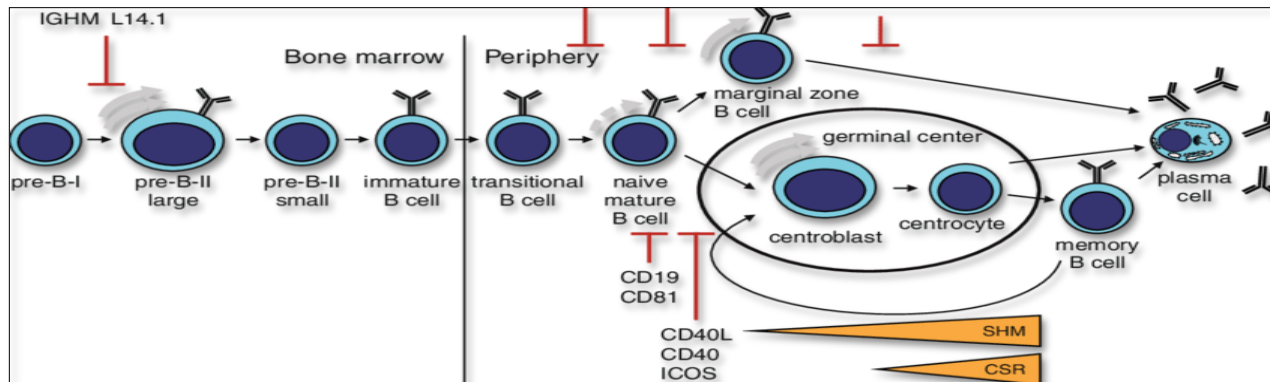
- The white blood cells (WBCs) involved in immunity are produced in the bone marrow.
- Many cells work together as part of the **innate** (non-specific) and **adaptive** (specific) immune system
- **Neutrophils** are the first responders of the innate immune system. Neutrophils and macrophages circulate through out the blood to identify and engulf the pathogens.
- The **Natural killer cells** , **T Lymphocytes** and **B Lymphocytes** are part of the adaptive immune system and are effector cells.
- **Effector cells are involved in destruction of cancer**



# Cells of the immune system

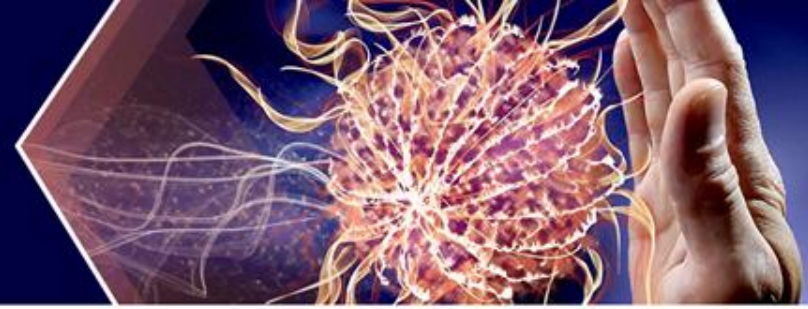


- There are two types of lymphocytes: B lymphocytes (**B cells**) & T lymphocytes (**T cells**)
- **B lymphocytes** mature in the bone marrow and then enter the circulation
- Plasma cells produce immunoglobulins (antibodies)
- Memory B cell retains the memory of the earlier antigenic exposure
- The immunity produced by B cells are termed as **Antibody/ Humoral immunity**

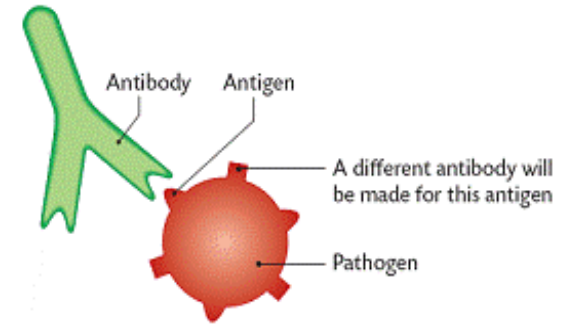




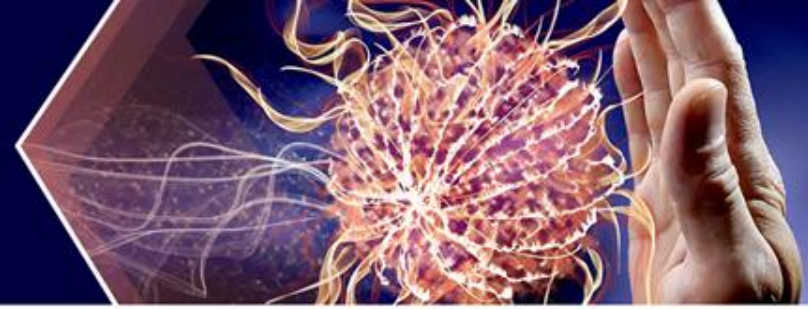
# Antigen and Antibody



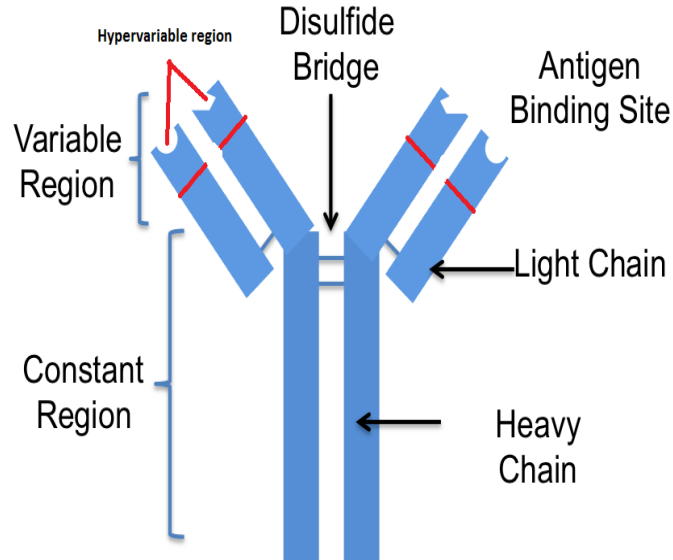
<b>ANTIGEN</b>	<ul style="list-style-type: none"><li>• Substance that is able to cause an immune response in the body</li><li>• Cells in the body, as well as CANCER cells, have antigens that can trigger an immune response</li><li>• Cancer / Tumor antigens trigger adaptive immunity</li></ul>
<b>ANTIBODY</b>	<ul style="list-style-type: none"><li>• Special proteins created by the WBCs that can kill / weaken the infection causing organism</li><li>• Each antigen will stimulate production of <b>one specific antibody</b> that will fit into its receptor area</li><li>• When a specific antibody binds to the <b>antigen on the surface</b> of a pathogen – it prevents the pathogen from entering the body</li></ul>



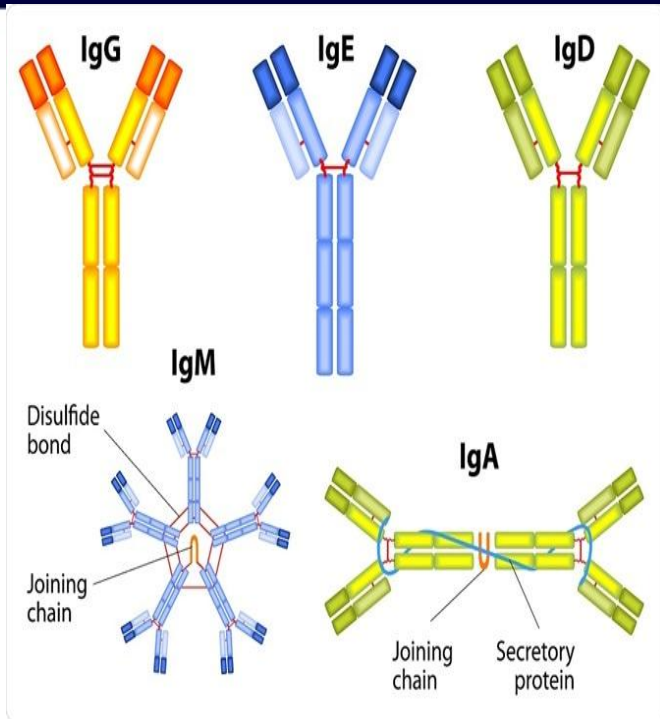
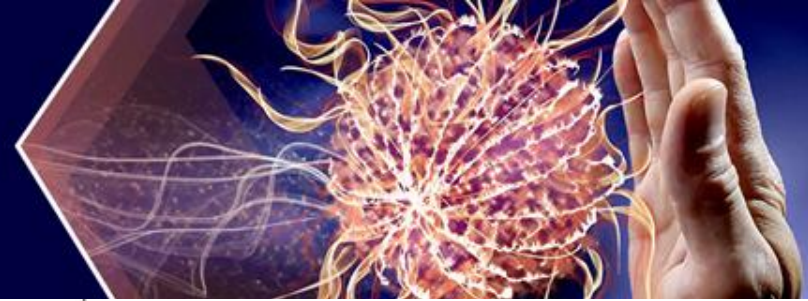
# Immunoglobulin/ Antibody



## Structure of Immunoglobulin



# 5 Classes of Immunoglobulins

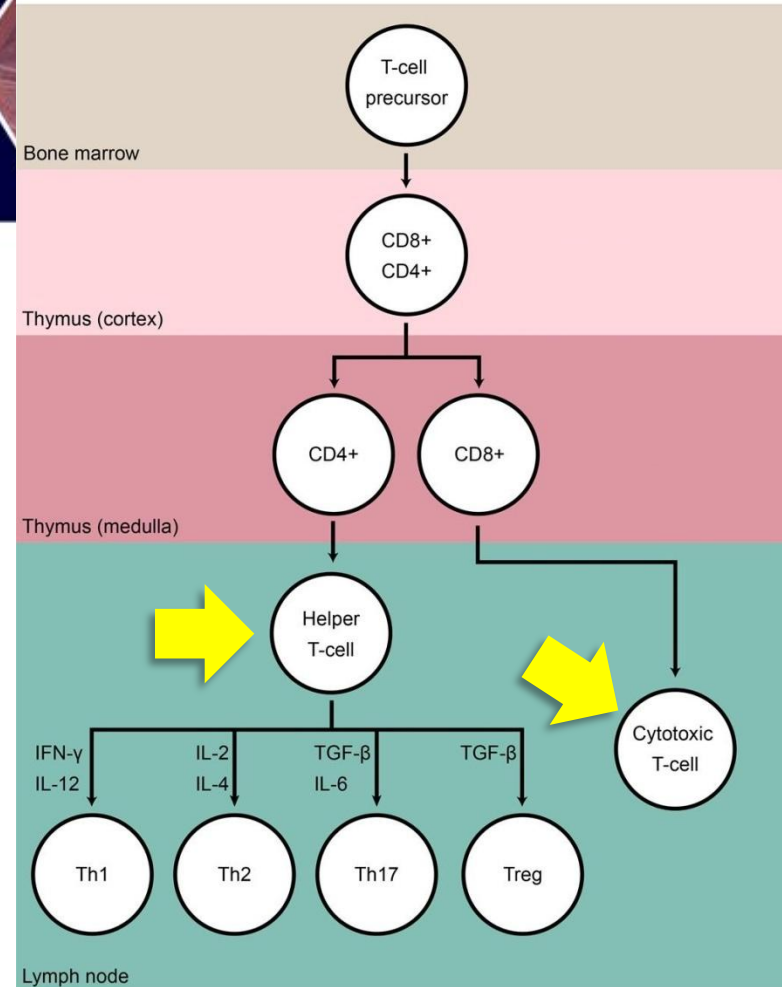


Class of Antibody	Serum levels	Structure	Biological functions
IgM	5%	Monomer Pentamer	Membrane-bound immunoglobulin on the surface of immature and mature B cells First antibody produced in a primary response to an antigen First antibody produced by the fetus Efficient in binding antigens with many repeating epitopes, such as viruses Classical complement activation
IgD	0.3%	Monomer	Membrane-bound immunoglobulin on the surface of mature B cells No biological effector function known
IgA	7-15%	Monomer Dimer	Predominant antibody class in secretions (saliva, tears, breast milk) and mucosa First line of defence against infection by microorganisms
IgG	85%	Monomer	Most abundant class with four isotypes - IgG1, IgG2, IgG3, IgG4 Crosses the placenta Opsonization
IgE	0.02%	Monomer	Defence against parasite infections Associated with hypersensitivity reactions (allergies) Found mainly in tissues

# T lymphocytes

- T lymphocytes move from the bone marrow to the thymus, where they mature into several kinds of cells with different functions.
- In the thymus – the T cells multiply and acquire different antigen receptors : CD4+ and CD8+ cells
- They then differentiate into **Helper T Cells** and **Cytotoxic T Cells**
- The T lymphocytes are regulators of adaptive function, serving as primary effectors for **cell-mediated immunity**.

## T-Cell Development





# Lymphoid Tissues

## Spleen:

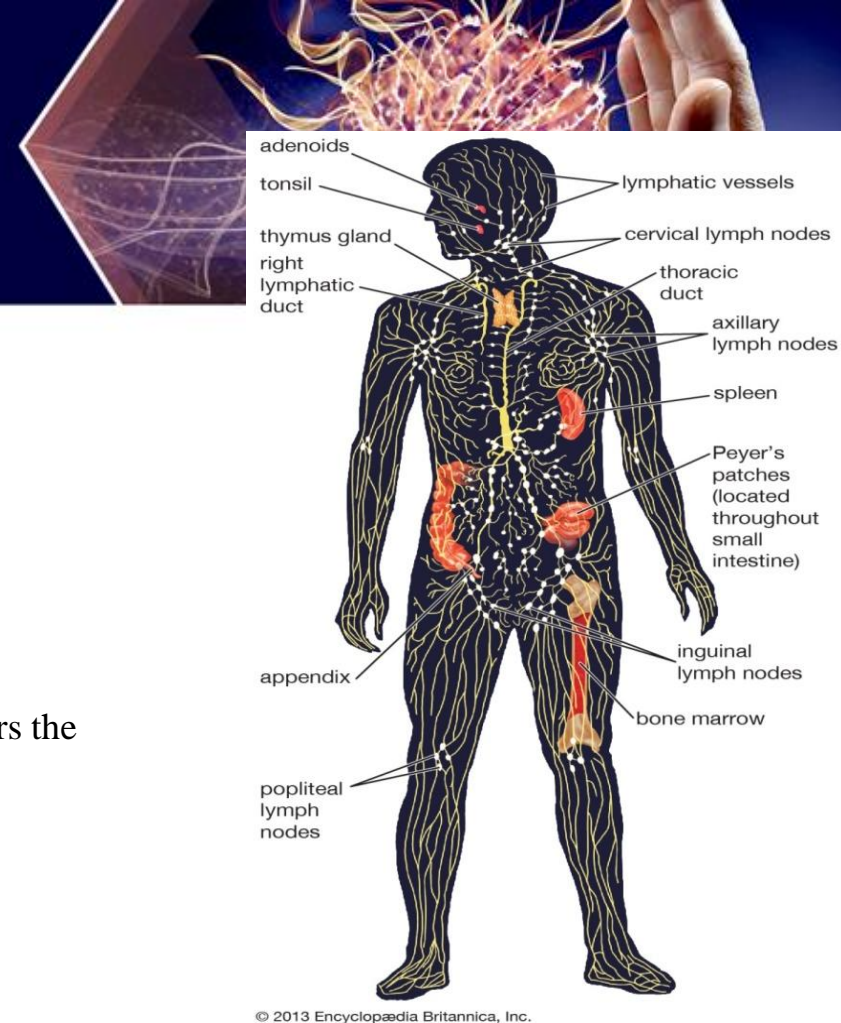
- Red pulp –site for the destruction of the old & injured RBCs.
- The white pulp contains concentrations of lymphocytes.

## Lymph nodes:

- Connected by lymph channels and capillaries
- Removes foreign material from the lymph system before it enters the bloodstream. Serves as center for immune cell proliferation.

## Mucosal immune cells

- Immune cells that **defend the body's mucosal surfaces** against microorganisms



# Two types of Immune Response

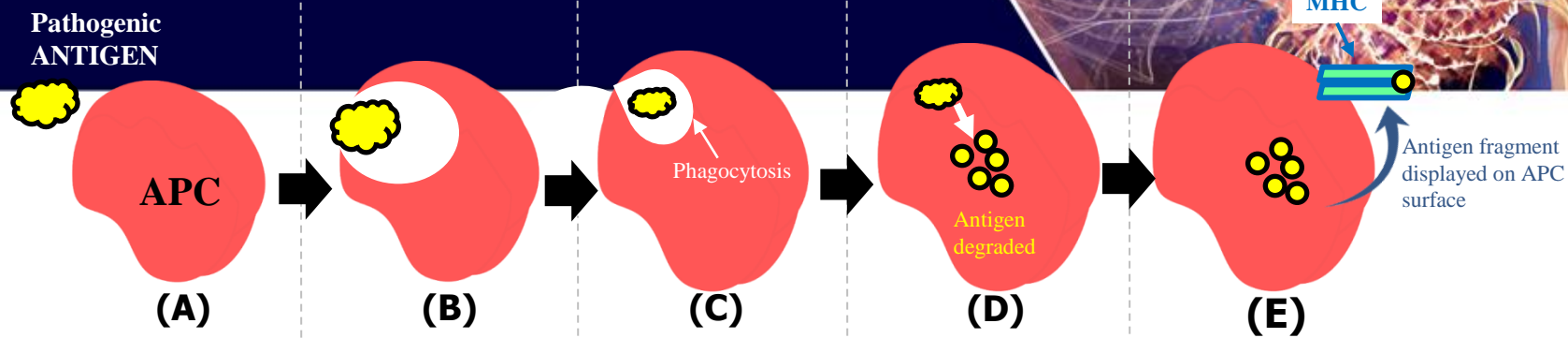


Parameter	Innate Immunity	Adaptive Immunity
Speed of Onset	Rapid first line of defense	Takes time to build an response
Specificity of Antigen	Low	High
Diversity of Response	Low	High
Potency	Low	High
Memory (Reacts quicker to subsequent exposures)	No	Yes
Example	Skin, hair, mucous membranes, phagocytosis by granulocytes, coughing	T and B lymphocyte response, inflammatory response

## Meaning of the parameters :

- **Speed of Onset** - How quick the immune response happens against any pathogen
- **Specificity of Antigen** - The power to identify different pathogenic antigens and destroy them
- **Diversity of Response** - The wider immune response possibilities
- **Potency** - The Strength of the response and durability / duration of immune response
- **Memory** -The ability to respond to a pathogen during subsequent or repeated exposures

# Antigen Presenting Cell (APC)



Commonly found APCs like **macrophages and dendritic cells**, detect pathogens, cancer cells

The APC then gets in contact with the pathogenic antigen

The antigen is ingested by the APC by a process called “**Phagocytosis**”

The ingested antigen is then degraded (**broken down**) inside the APC

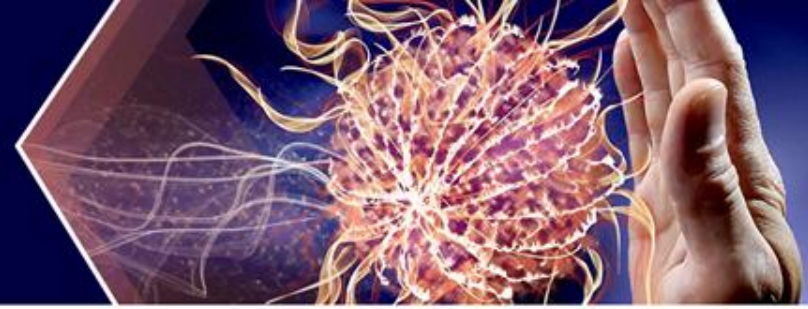
One of the fragments (peptide) from the broken down antigen is then “*displayed*” on the surface of the APC – by help of an “*arm*” or “*Platform*” called **Major Histocompatibility Complex (MHC)**. This helps the circulating T cells to identify the antigen and initiate adaptive immune response by **activation of the T cell**

## 2. INTRODUCTION TO IMMUNO-ONCOLOGY





# Definitions



- **Immuno-Oncology therapy** is a unique approach that uses the **body's immune system** to help fight cancer
- **Immunotherapy** is defined as the approach to treat cancer by generating or augmenting an immune response against it
- **Immune modulation** is based on stimulation of T-cell function with antibodies that block or activate regulatory receptors to suppress the tumor growth

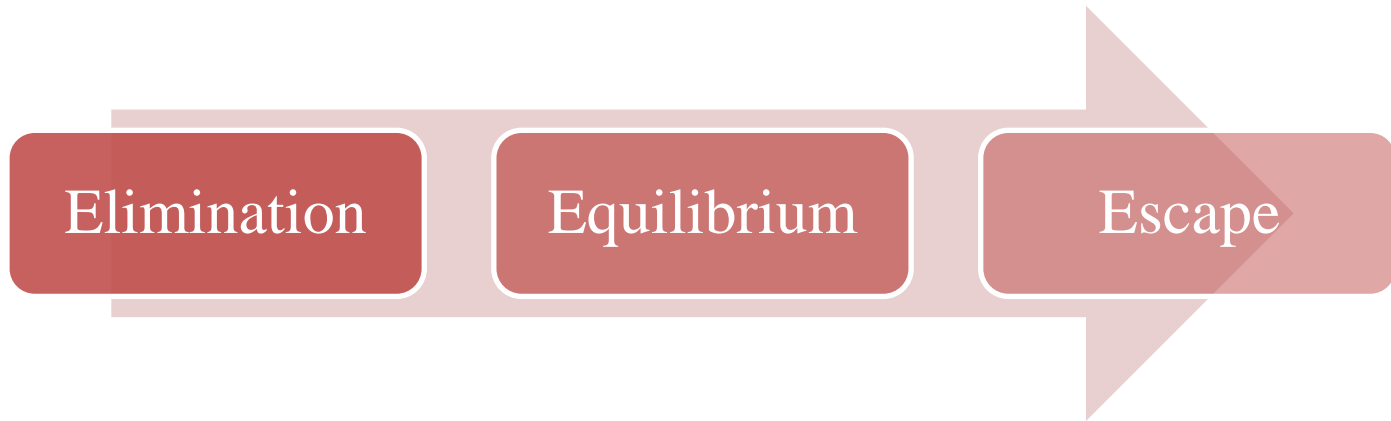
# CANCER AND THE IMMUNE SYSTEM: A DYNAMIC RELATIONSHIP



## Immunoediting Process

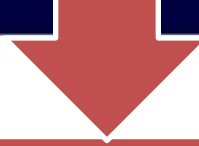
The immune system regulates tumour growth through a dynamic process, in which it can either **block tumour growth, development and survival** or may promote **tumour progression**

## Stages :



## Elimination phase

Cancer cells are identified and destroyed long before they become clinically apparent (i.e. immune protection) and the host remains free of cancer



## Equilibrium phase

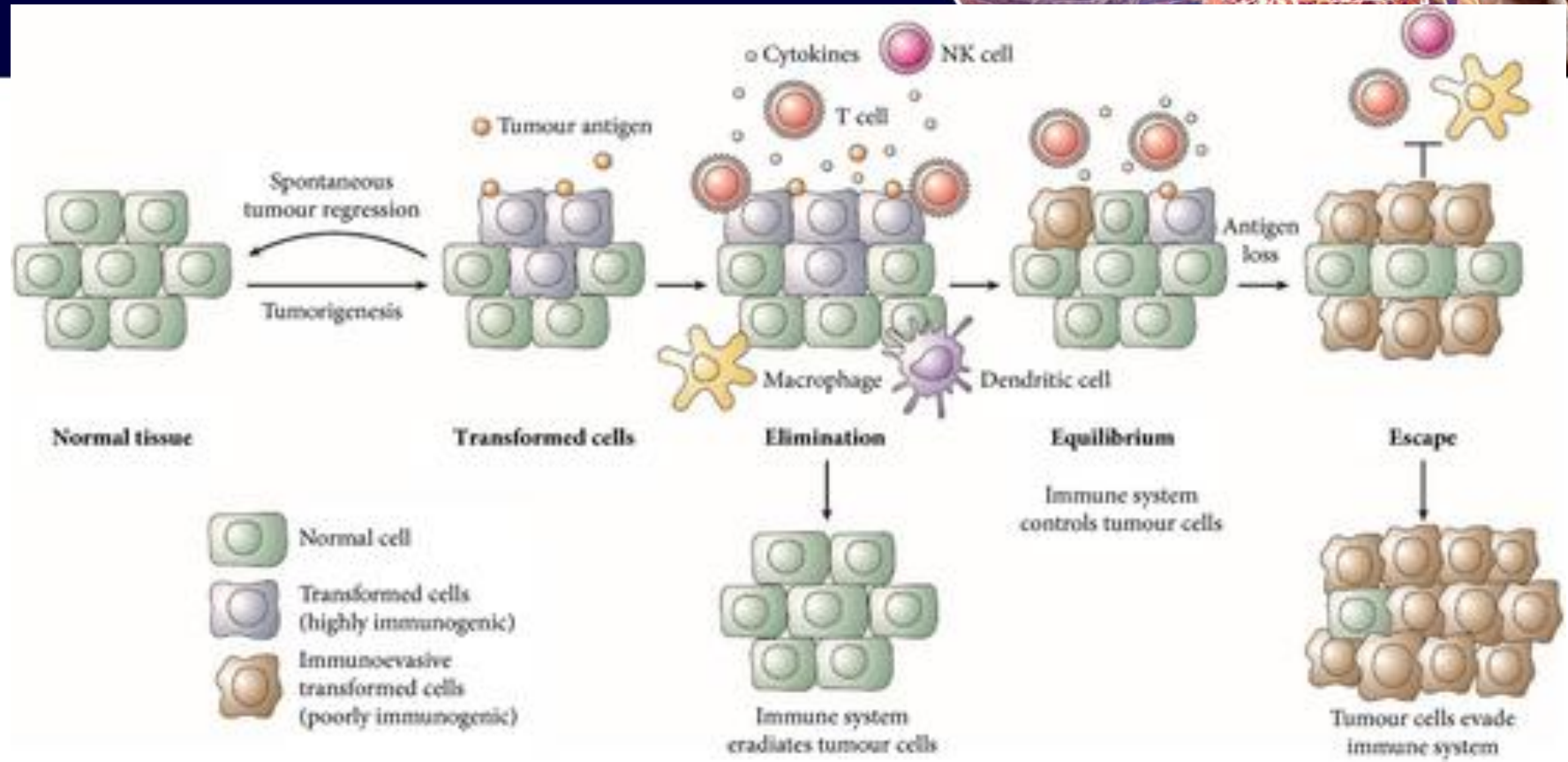
If a cancer cell variant is not destroyed, the cancer cells persist but outgrowth is prevented by the immune system. This stage lasts for many years or even the lifetime of the host



## Escape phase

Outgrowth of cancer cells is no longer controlled by the immune system, leading to clinically apparent and progressive disease (immune evasion)

# CANCER IMMUNOEDITING PROCESS

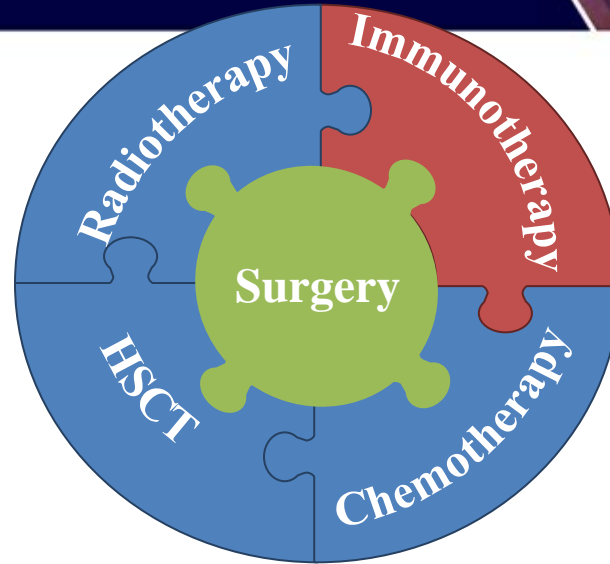
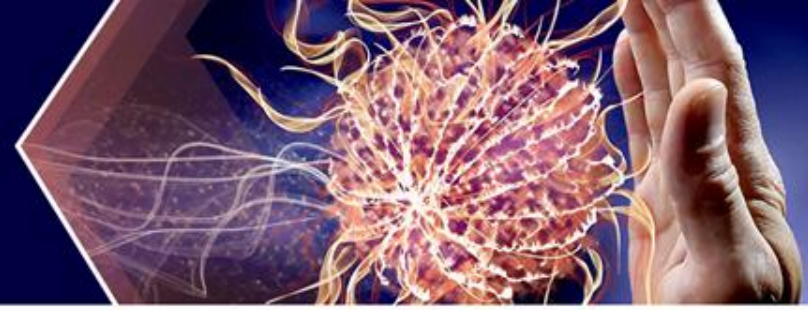




### 3. HISTORY & FEATURES OF IMMUNOTHERAPY



# Cancer treatment landscape



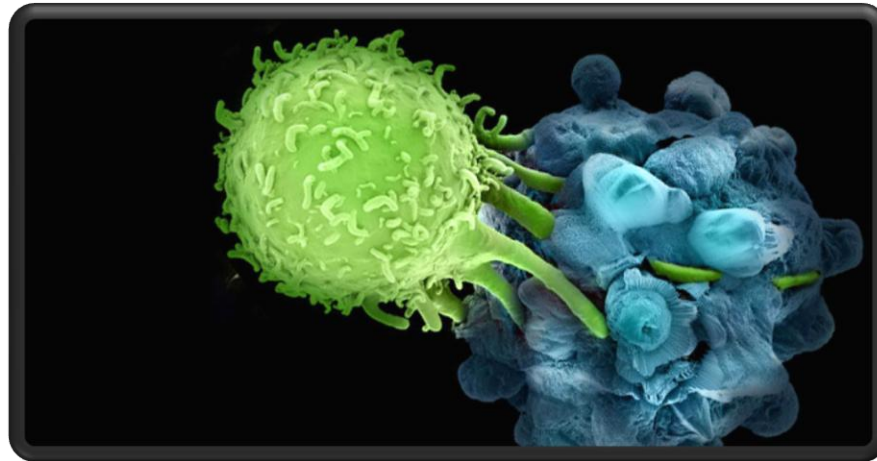
Immuno-Oncology / Cancer immunotherapy is an emerging treatment modality that aims to **work with the body's immune system to fight cancer**

# Definition



Immunotherapy refers to any treatment that boosts or restores the ability of the immune system to fight cancer, infections and other diseases

*-National Cancer Institute*



# Breakthrough in Cancer Immunotherapy

1890s  
Coley  
First  
cancer  
vaccine  
(bacterial  
toxin)

1959  
BCG  
for  
cancer  
therapy

1992  
IL-2  
appro-  
ved for  
renal  
cell  
cancer

2001  
concept  
of  
'Immuno  
editing'

2011 first  
check point  
inhibitor  
Ipilimumab  
for  
metastatic  
melanoma

2015  
Anti  
PD-1  
Nivolu  
mab for  
Lung  
cancer

1909  
Hypothe-  
sis on  
cancer  
Immuno  
surveill-  
ance

1985  
Adoptive  
cell  
transfer  
for cancer

1997 First  
mono  
clonal  
antibody  
Rituximab

2010  
first  
approved  
cancer  
vaccine  
Sipuleuc  
el -T for  
prostate  
cancer

2014  
CAR T  
cell  
therapy  
response  
(92%)

2020  
FDA  
approves  
multiple  
immuno-  
therapeu  
tic drugs

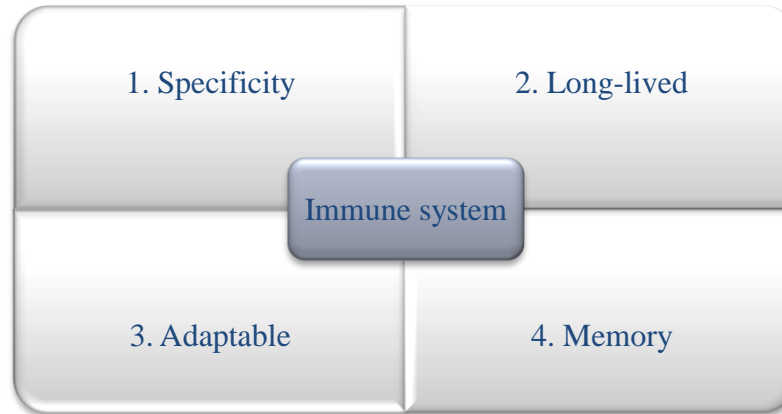


# Features of Immunotherapy



- Immunotherapy targets the cancer cells sparing the normal cells

**Immunotherapy is a preferred treatment for cancer due to:**



# Features of Immunotherapy



It can **precisely attack** tumor cells, potentially throughout the body (with a few exceptions), thus minimizing damage to surrounding tissue

1. Specificity

2. Long-lived

Immune  
system

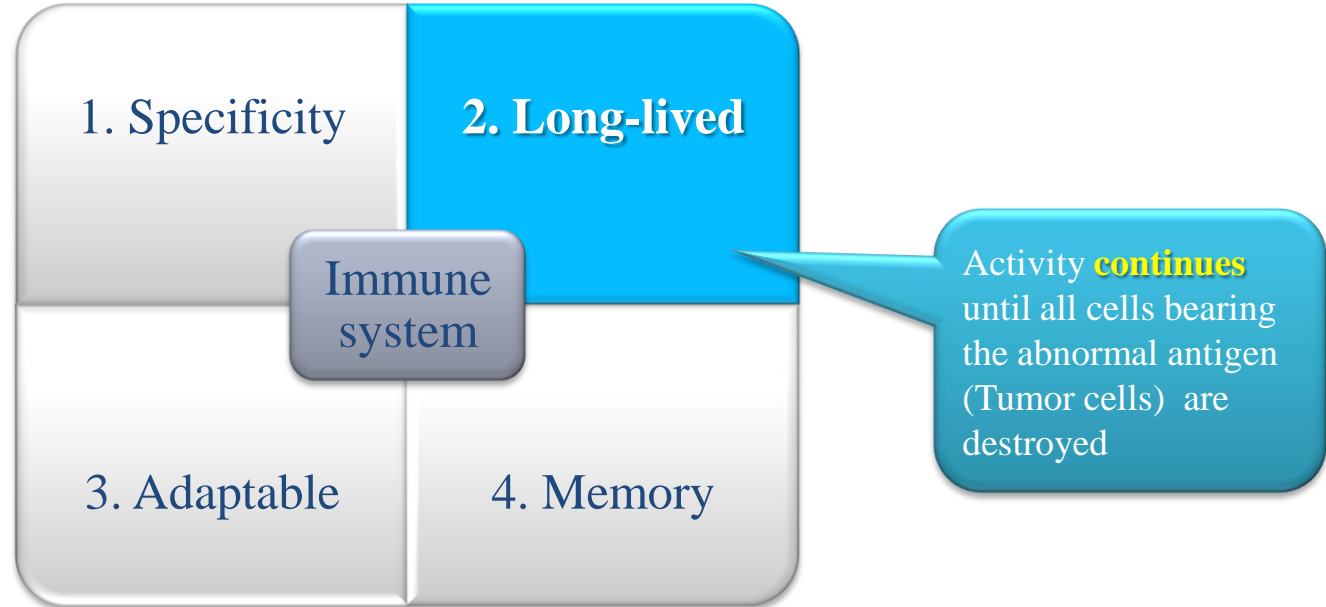
3. Adaptable

4. Memory

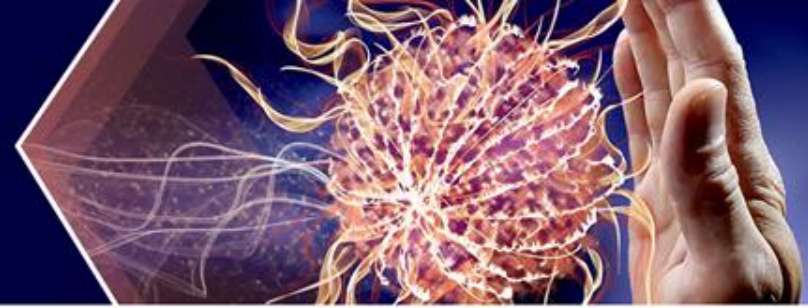
# Features of Immunotherapy



**Immunotherapy is a preferred treatment for cancer due to:**



# Features of Immunotherapy



**Immunotherapy is a preferred treatment for cancer due to:**

1. Specificity

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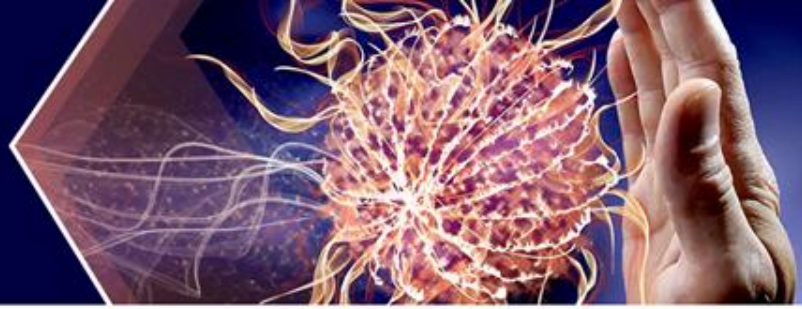
Immune  
system

3. Adaptable

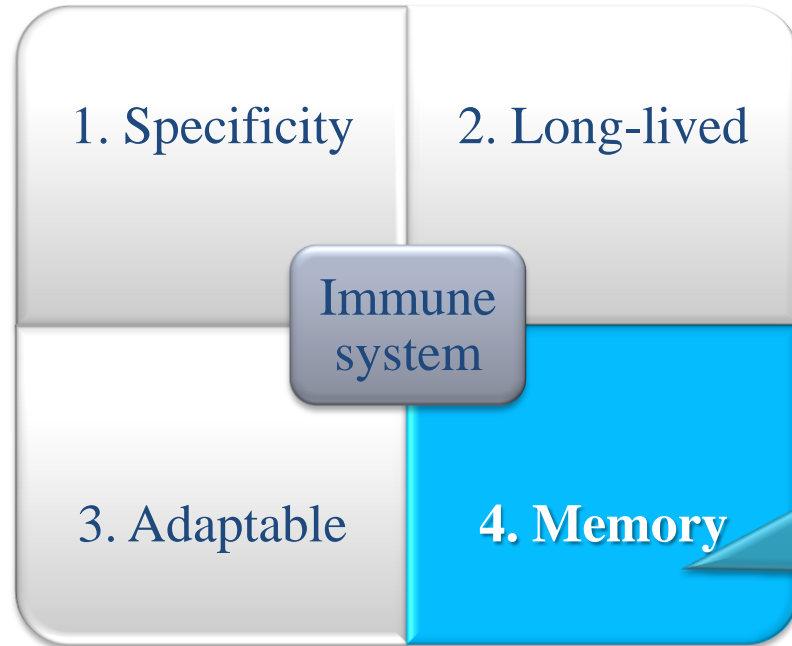
4. Memory

It may be effective in **different types** of cancer, regardless of specific tumor characteristics; can adjust the size and type of its response

# Features of Immunotherapy



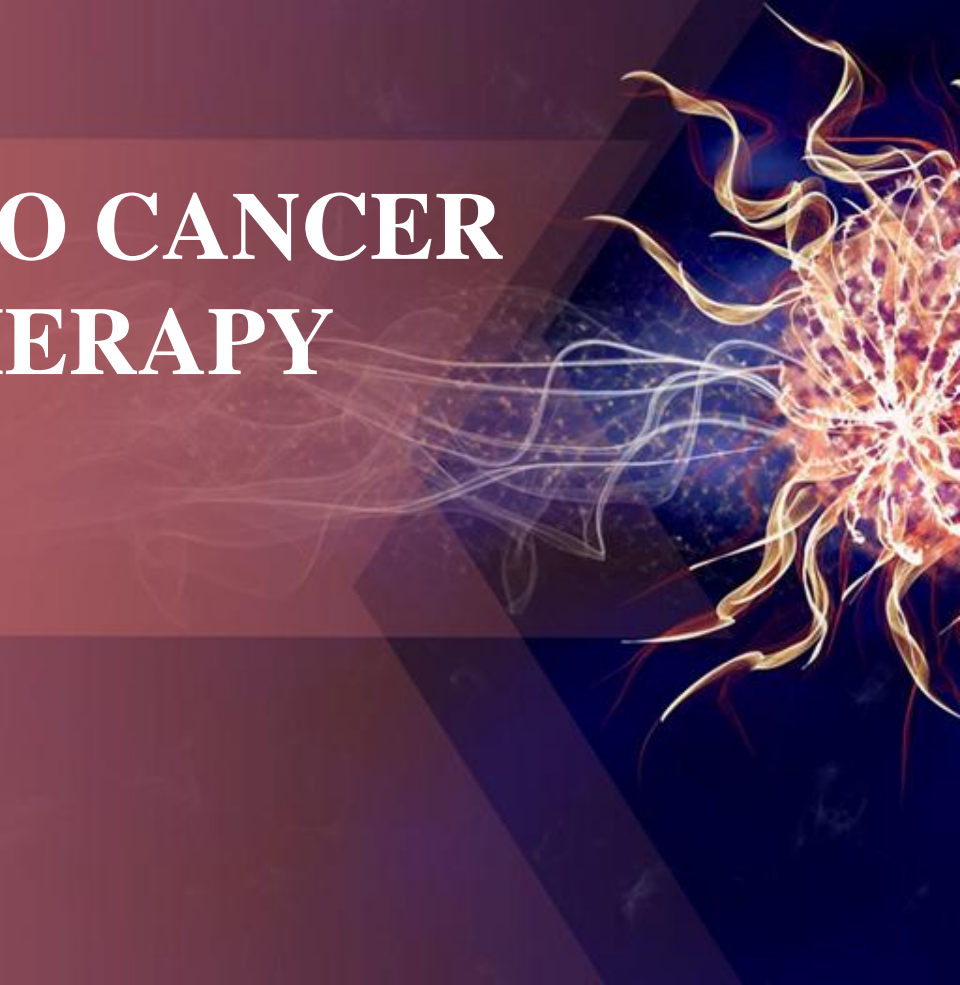
**Immunotherapy is a preferred treatment for cancer due to:**



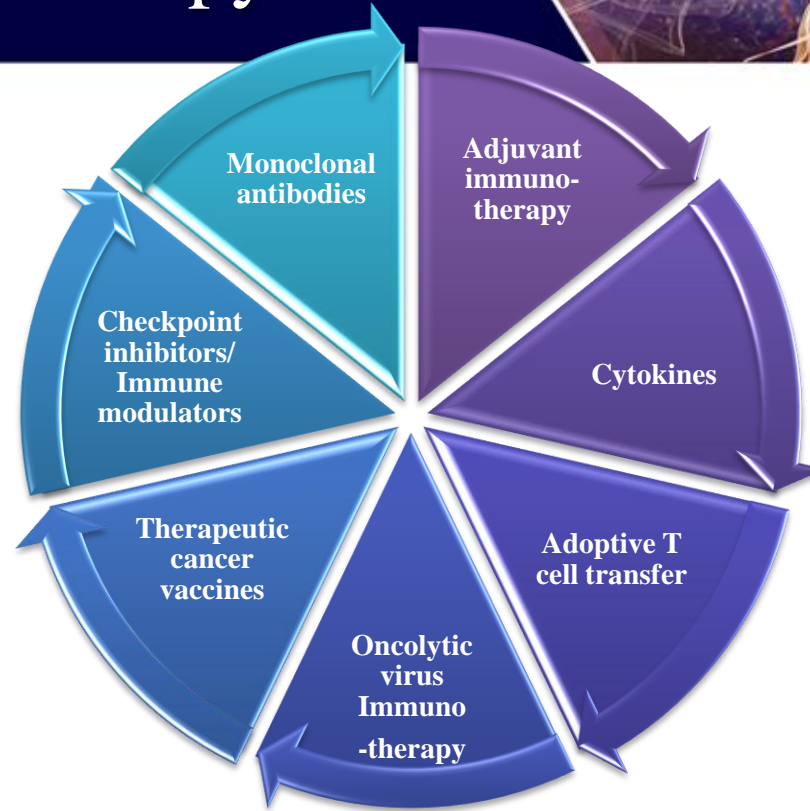
It **remembers** antigens and mounts a faster and stronger response on **repeated exposure** to them, theoretically protecting from tumor recurrence



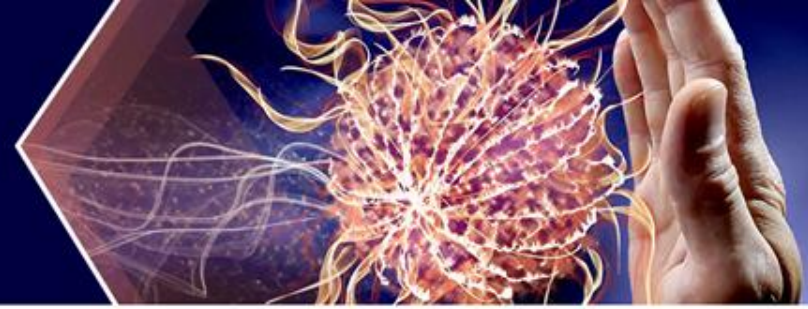
# 4. APPROACHES TO CANCER IMMUNOTHERAPY



# Approaches to cancer immunotherapy



# IMMUNOTHERAPY: MECHANISM OF ACTION



## 1. Activation of effector immune cells

Vaccines

## 2. Stimulatory strategies

Adoptive cellular  
therapy

Oncolytic virus

## 3. Strategies to neutralize immunosuppressor mechanisms

Monoclonal  
antibodies

Immune check point  
inhibitors

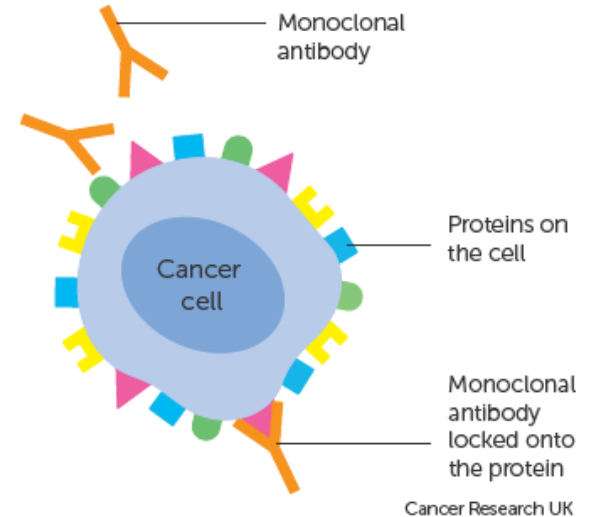
# 1. MONOCLONAL ANTIBODIES



- Monoclonal antibodies work in cancer via several different mechanisms of action, which generally involve binding to a specific target antigen and thereby inducing cell death.

Some of the mechanisms include:

- Blocking the signalling pathways needed for tumour cell growth
- Triggering an immune-mediated cytotoxic response (e.g. antigen-dependent cellular cytotoxicity)
- Blocking angiogenesis



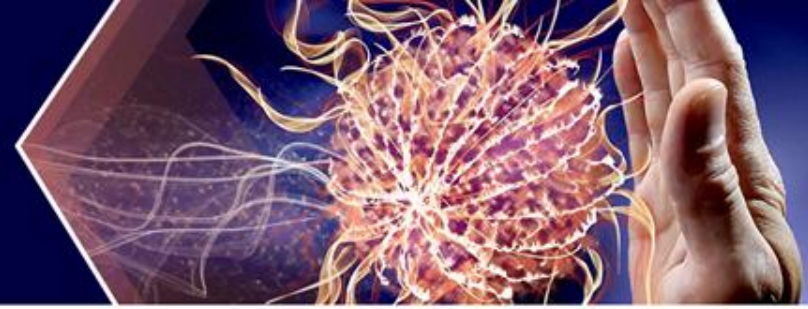
# Common Monoclonal antibodies



Rituximab	Rituxan	CD20	Relapsed or refractory, low-grade or follicular, CD20 <sup>+</sup> NHL
Tositumomab and I-131 tositumomab <sup>a</sup>	Bexxar	CD20	Refractory to rituximab, relapsed, CD20 <sup>+</sup> follicular NHL
(90)Y-ibritumomab tiuxetan <sup>b</sup>	Zevalin	CD20	Relapsed or refractory, low-grade, or transformed B-cell lymphoma
Alemtuzumab	Campath-1H	CD52	Salvage B-cell CLL
Gemtuzumab ozogamicin	Mylotarg	CD33	Relapsed acute myeloid leukemia
Trastuzumab	Herceptin	HER-2/neu	HER-2 <sup>+</sup> metastatic breast cancer
Bevacizumab	Avastin	VEGF	Metastatic colorectal cancer, frontline with 5-FU
Cetuximab	Erbitux	EGFR	Second line for metastatic colorectal cancer in combination with irinotecan



## 2.CYTOKINES

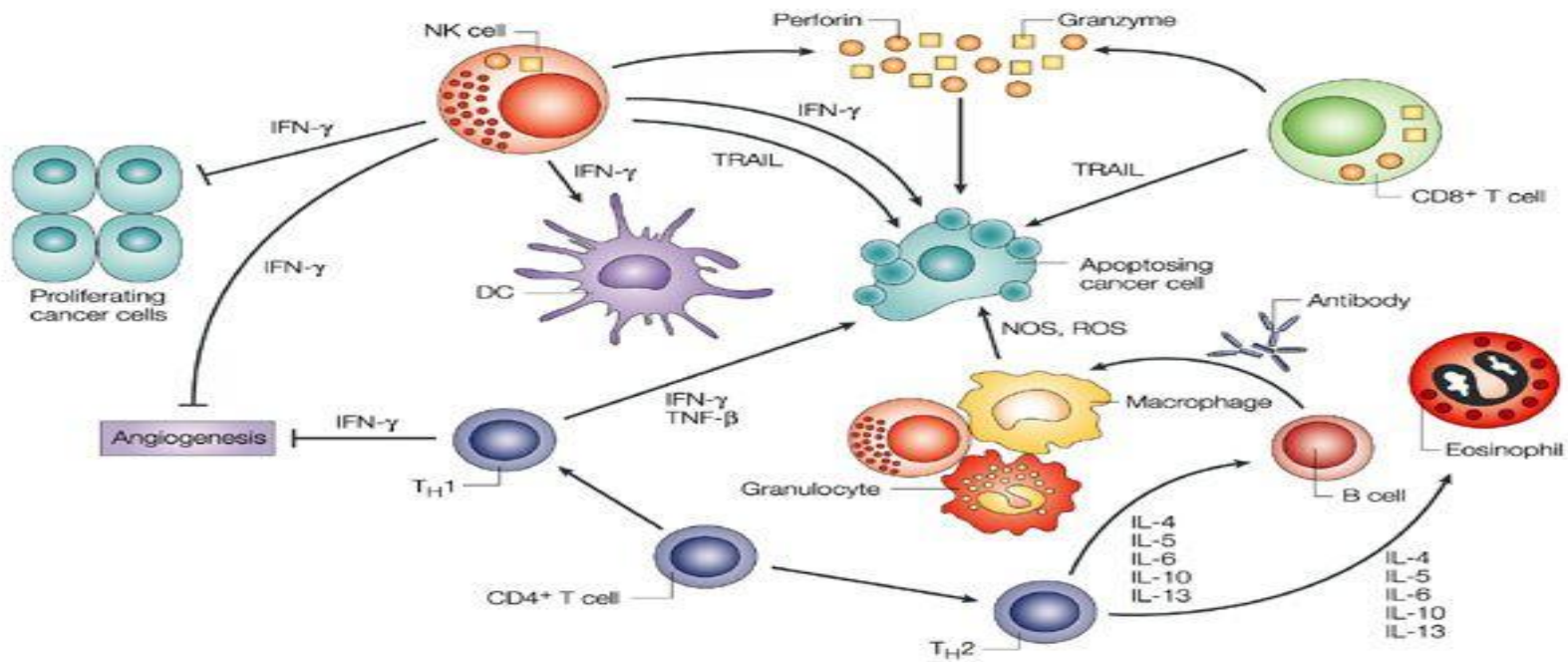


- Cytokines are **protein molecules** that help **regulate and direct the immune system**. Cells release cytokines, which act as **messengers** to other cells, telling them when and where to launch an immune response.
- Various types of cytokines are naturally produced by the body.
- In cancer treatment, cytokines are synthesized in the lab and injected in larger doses than the body would normally produce.



- **Interleukin 2 (IL-2)** is designed to **target adaptive immune cells**, such as T-cells and B-cells, to respond to tumors. IL-2 may help the body produce **antigen-fighting T-cells** and **stimulate B-cells to produce more antibodies**.
- Side effects: Weight gain, low blood pressure, flu-like symptoms.
- **Interferon-alpha (IFN-alpha)** helps the **body generate innate immune cells**, such as **dendritic cells** and **macrophages**, that are designed to attack unhealthy cells  
Side effects: Flu-like symptoms, an increased risk of infection, rashes, and thinning hair.

# Cytokines-Mechanism of action



# CYTOKINES IN CANCER TREATMENT



- Renal cell carcinoma (IL-2, IFN-alpha)
- Melanoma (IL-2, IFN-alpha)
- Hairy cell leukemia (IFN-alpha)
- Follicular non-Hodgkin's lymphoma (IFN-alpha)
- Cutaneous (skin) T cell lymphoma (IFN-alpha)
- Chronic myelogenous leukemia (IFN-alpha)
- Kaposi's sarcoma (IFN-alpha)

### 3. CHECKPOINT INHIBITORS



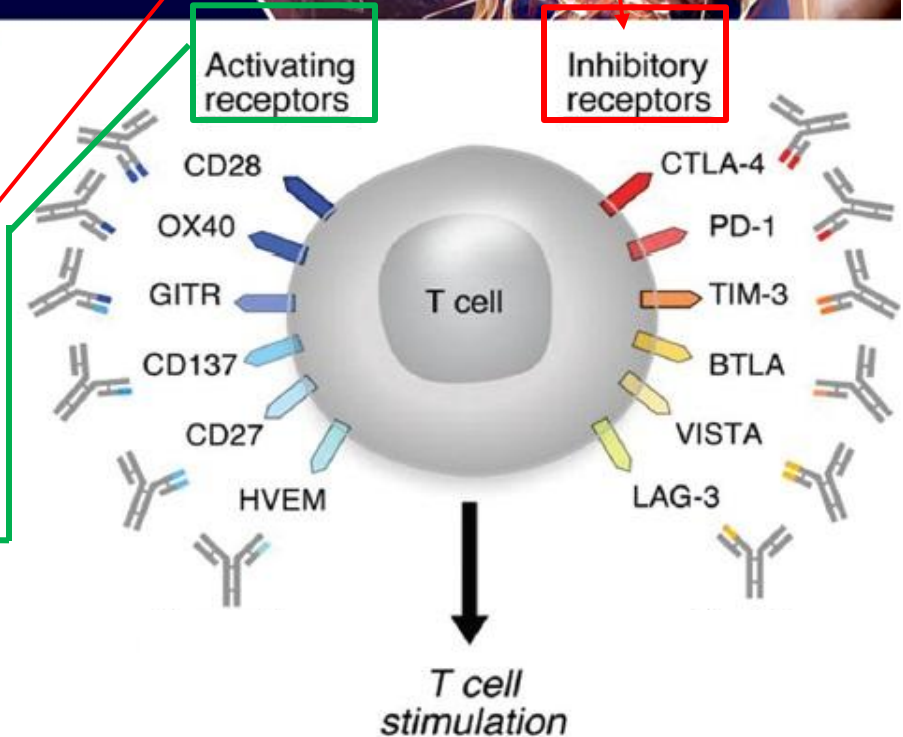
- An important function of the immune system is its ability to recognize between normal cells and “foreign” (self and non-self)
- This mechanism destroys the foreign cells while sparing the normal cells.
- **Immune checkpoints** are molecules on certain immune cells that need to be **activated** (or **inactivated**) to start an immune response.
- Cancer cells sometimes find ways to *use these checkpoints* **to avoid** being attacked by the immune system



# Checkpoints & their actions



- There are different types of checkpoint proteins present on the T cell. Broadly they have two actions (a) **Activation** or (b) **Inhibitory**
- Any signal through the **inhibitory receptors** of the T cell → Inhibits the T cell and thus the T cell will **NOT ATTACK** that particular cell (eg. cancer cell)
- Similarly, any signal through the **activating receptors** of T cell → activates the T Cell and thus the T cell **WILL ATTACK** that particular cell (eg. cancer cell )

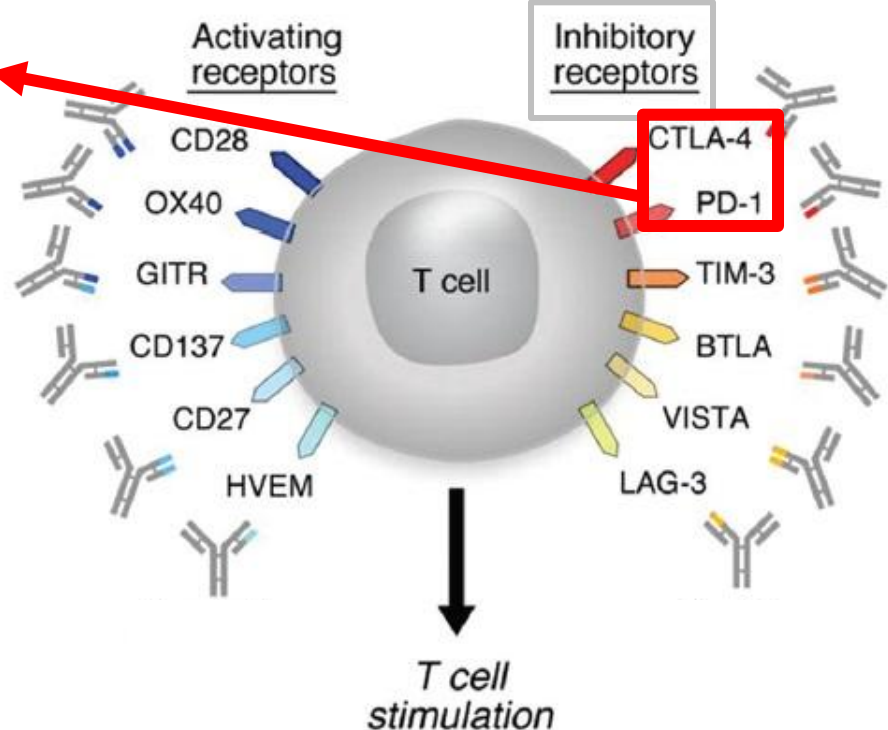


# Different types of Checkpoints and their actions

- Currently the **important Inhibitory receptors** are :
- **PD-1** (Programmed Cell Death Protein 1) and
- **CTLA4** (Cytotoxic T Lymphocyte Antigen 4)

- The **PD1** receptors bind with **PDL1** ligand on APC / Tumor cell
- **CTLA4** receptors bind with **B7** ligand on APC / Tumor cell

- Once they bind , they **INHIBIT the T Cell from acting** against the cancer / tumor cell
- Thereby leading to growth of the cancer cells

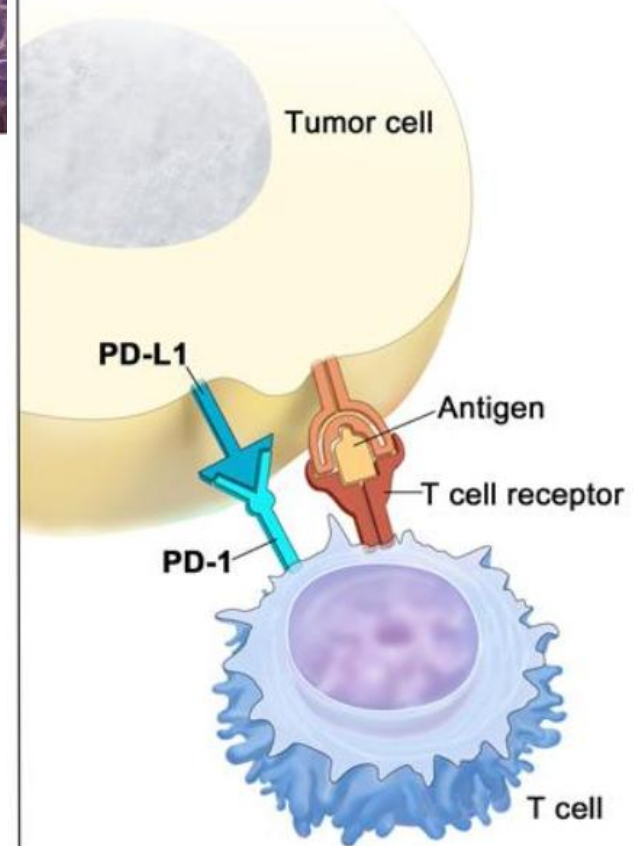


Source : Mellman I et al. *Nature*. 2011;480:480-489.

# PD1-PDL1 Checkpoint

- When PD-1 (in T cell) binds with PD-L1 receptor in the tumor cell → It basically inhibits (**NOT TO ATTACK**) the T cell; so ultimately the tumor cell is not attacked by the T cell
- Some cancer cells have large amounts of PD-L1 , which helps the tumor cells **HIDE** from an immune surveillance

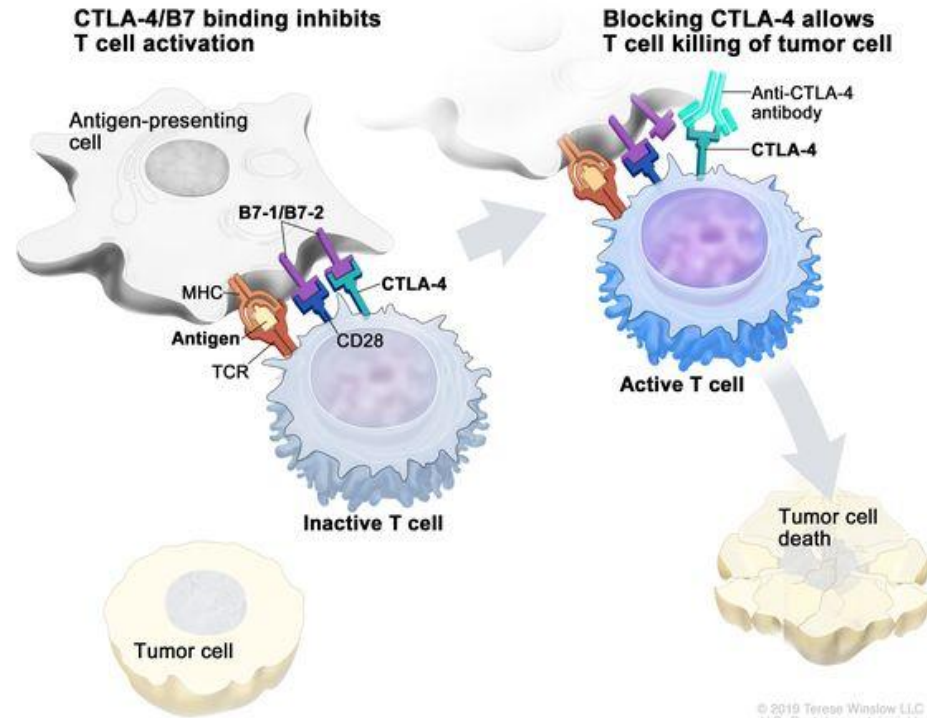
PD-L1 binds to PD-1 and inhibits T cell killing of tumor cell



# CTLA4 Checkpoint



- CTLA4 is another checkpoint
- When CTLA4 (on the T cell) binds to the B7 ligand on the APC or Tumor cell → It basically tells the T cells **NOT TO ATTACK** the tumor cells
- Hence the cancer cells begin to grow and increase inside the body and cancer spreads

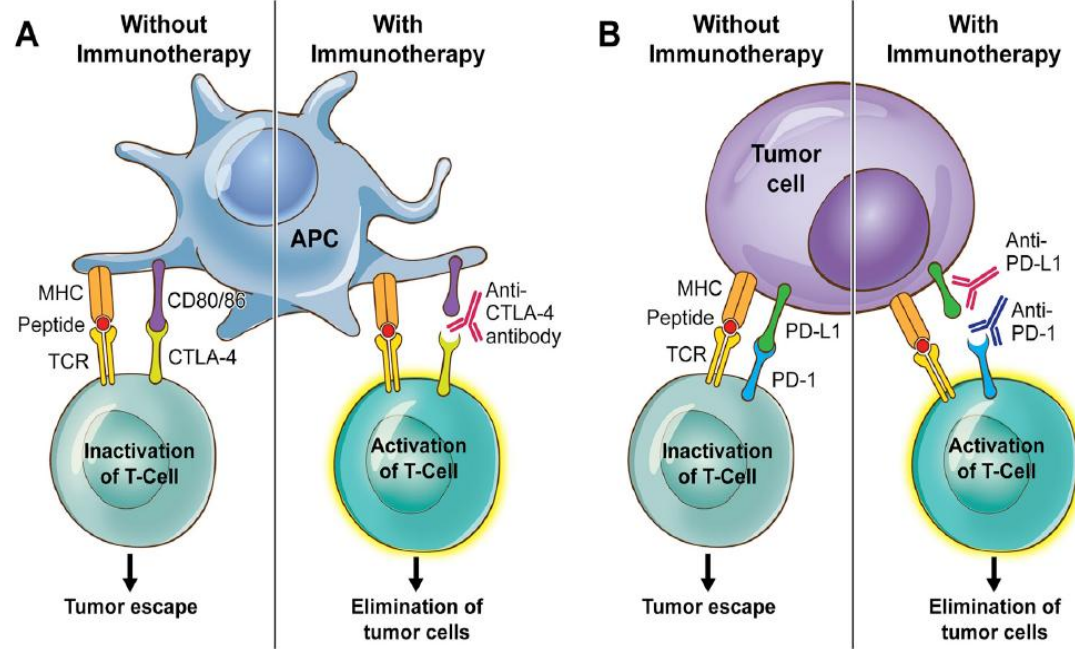




# Checkpoint INHIBITORS



- Monoclonal antibodies **block this binding (PD1 - PDL1) (CTLA4 – CD 80 / 86)** and boost the immune response **AGAINST** cancer cells



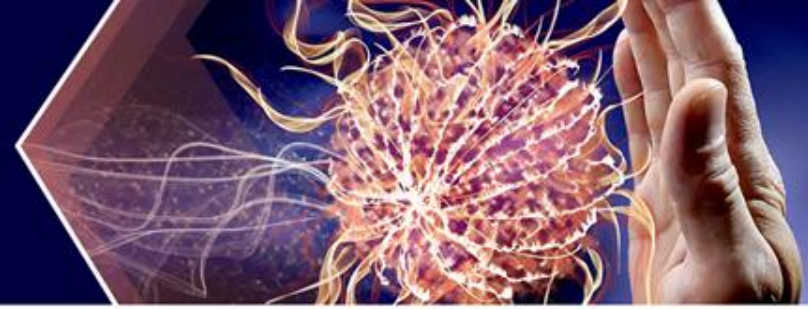


# Checkpoint Inhibitor drugs currently approved for use in India



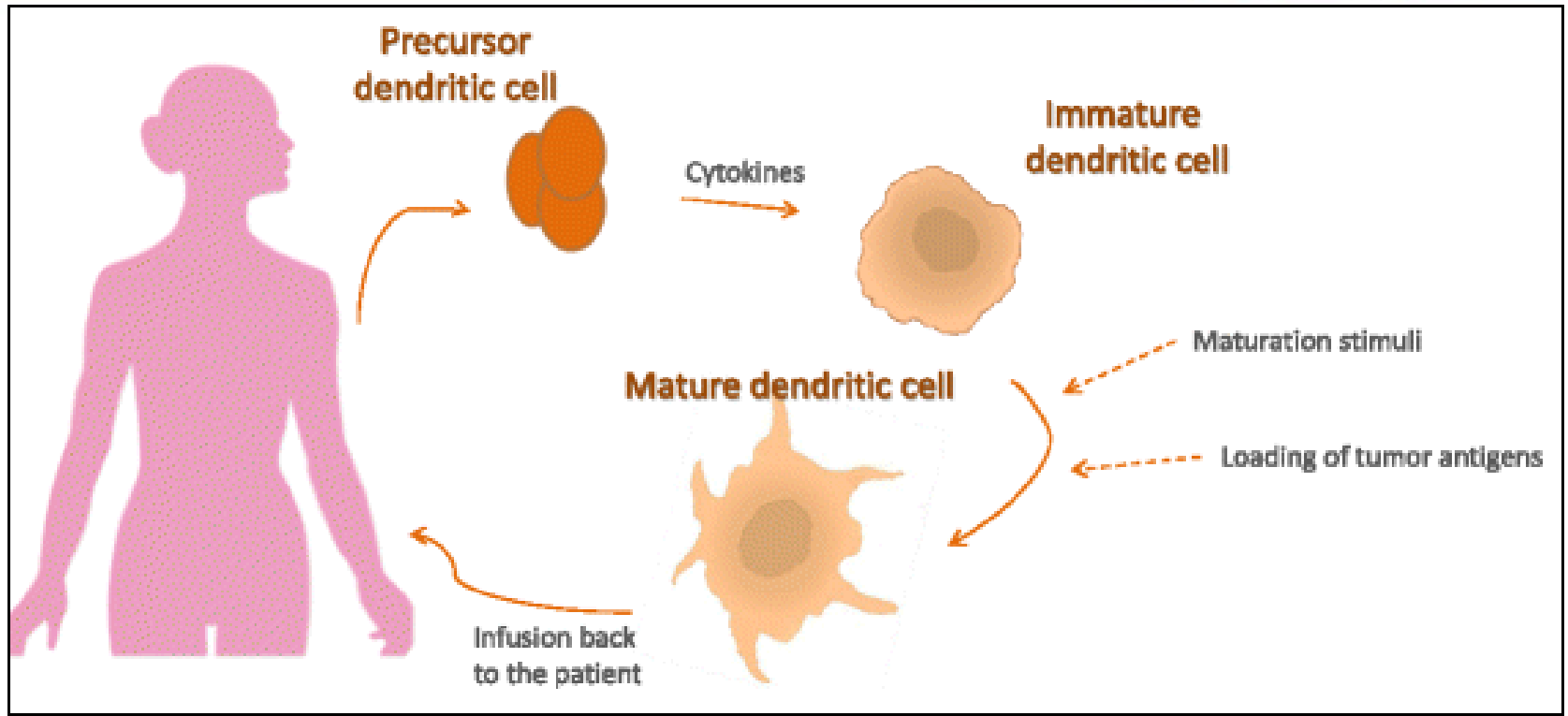
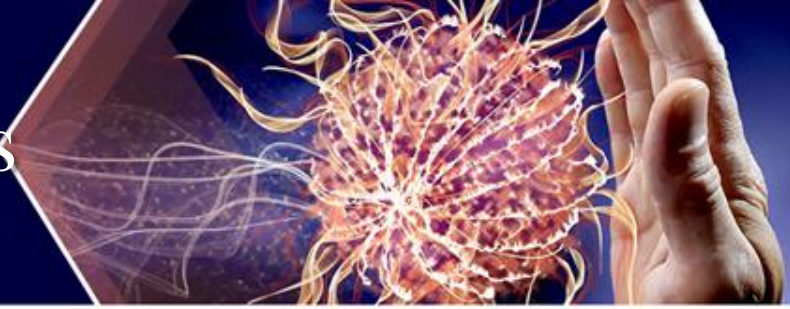
Class of Checkpoint Inhibitors	Molecule name	Brand Name (India)
<b>Anti PD-1</b>	Nivolumab	Opdyta®
	Pembrolizumab	Keytruda®
<b>Anti PD-L1</b>	Atezolizumab	Tecentriq®
	Durvalumab	Imfinizi®
<b>Anti CTLA4</b>	Ipilimumab	Yervoi®

## 4. THERAPEUTIC CANCER VACCINES



- **Primary goal:** is not to prevent disease but to **target the immune system** to help **initiate or enhance** an active immune response (activate the immune system with **targeted T cells** to seek out and destroy target cancer cells) against an existing cancer.
- Proven to improve overall survival in patients with **prostate cancer (Sipuleucel-T)**
- **Cancer prevention: HPV vaccines** (Gardasil® & Cevarix®)

# Dendritic cell based vaccines

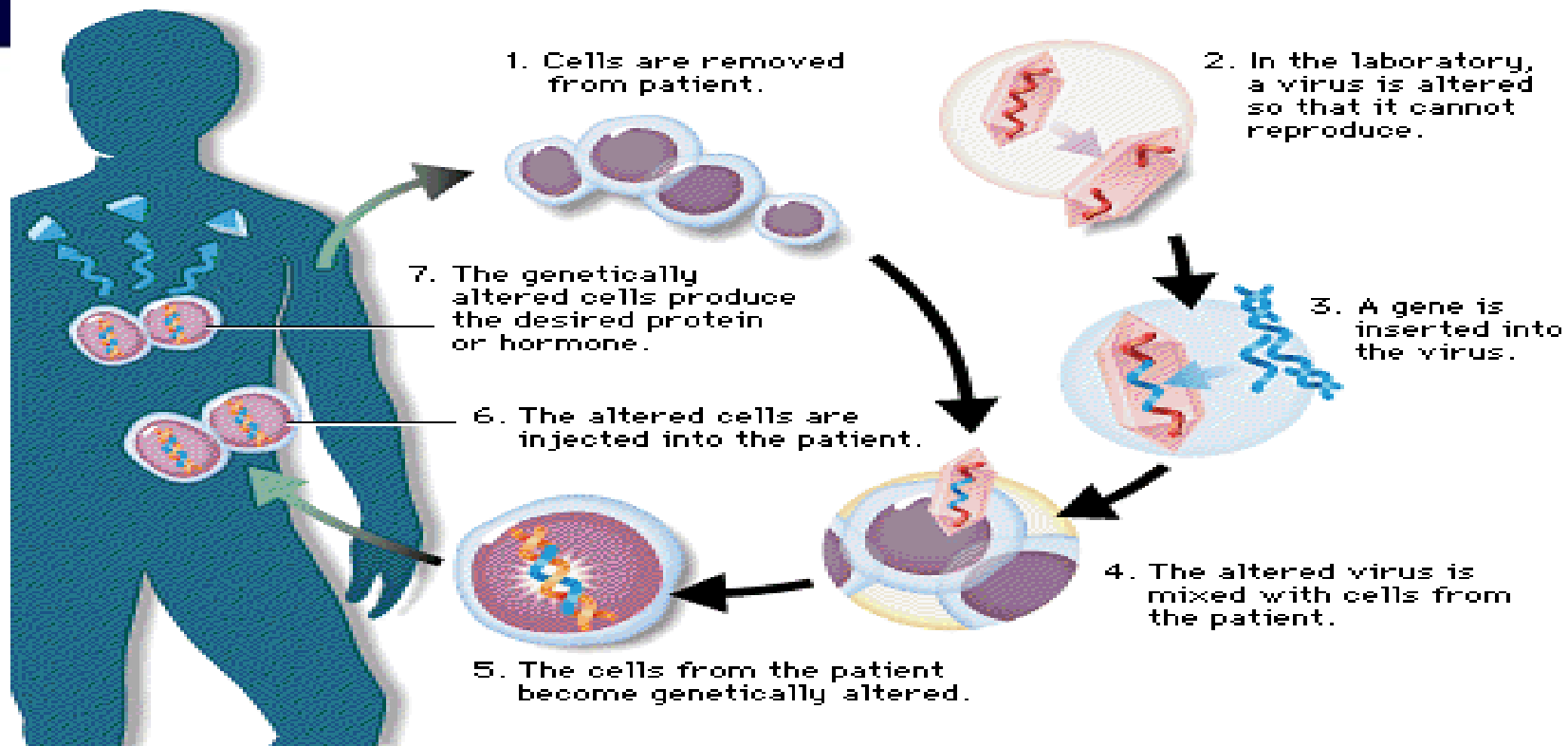


## 5. ONCOLYTIC VIRUS IMMUNOTHERAPY



Viruses can be engineered to efficiently infect cancer cells preferentially over normal cells, to promote presentation of tumor-associated antigens, to activate "danger signals" that promote a less immune-tolerant tumor microenvironment, and to serve as transduction vehicles for expression of immune modulatory cytokines

# ONCOLYTIC VIRUS THERAPY





## 6. ADOPTIVE T CELL TRANSFER



Broadly refers to the practice of **manipulating patient-specific T cells** ex vivo to make them more reactive to specific antigens

### **Chimeric antigen receptors:**

- (CAR) T cells are **genetically modified T cells**
- Patient's own T cells are manipulated ex vivo to express the antigen-binding domain from a B cell receptor that is fused to the intracellular domain of a CD3 T cell receptor (CD3-zeta).
- As a result, **recognition of a specific cell surface antigen** activates T cell response independently of MHC recognition.
- Various modifications can enhance CAR effector function, such as co-expression of intracellular costimulatory domains such as CD28 or 4-1BB (CD137) or pro-effector cytokines such as IL-12

# CAR T- CELL PROCESS



## LEUKAPHERESIS

Collect patient's white blood cells



## MANUFACTURING PROCESS

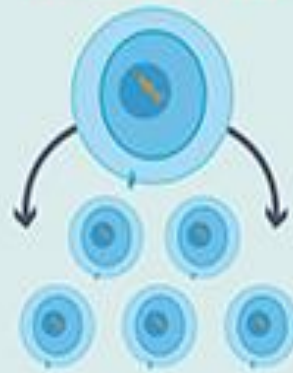
Isolate and activate T cells



Engineer T cells with CAR gene



Grow and expand number of T cells



## INFUSION

Infuse same patient with engineered T cells



## 7. ADJUVANT IMMUNOTHERAPY



- Adjuvant immunotherapies are substances that are either used alone or combined with other immunotherapies to **boost the immune response even more**
- Adjuvant immunotherapies can improve responses to therapeutic cancer vaccines that require the work of T cells or other immune cells
- Some adjuvant immunotherapies use ligands—molecules that can bind to protein receptors—to boost immune responses
- Eg. Bacillus Calmette-Guérin (Bladder cancer)
- **GM-CSF + Vaccines** → prostate & pancreatic cancer

# COMBINATION THERAPY



- The combination of different treatment methods holds significant potential to improve treatment outcomes
- **Chemoimmunotherapy**- synergistic effect (chemo + CTLA-4 blockade agents)
- **Radiation +Immunotherapy**- potentiates the systemic efficacy of immunotherapy & enhances the local efficacy of radiation therapy
- **Hormonal therapy + Immunotherapy**- androgen ablation

## 5. IMMUNE RELATED ADVERSE EVENTS (irAE)





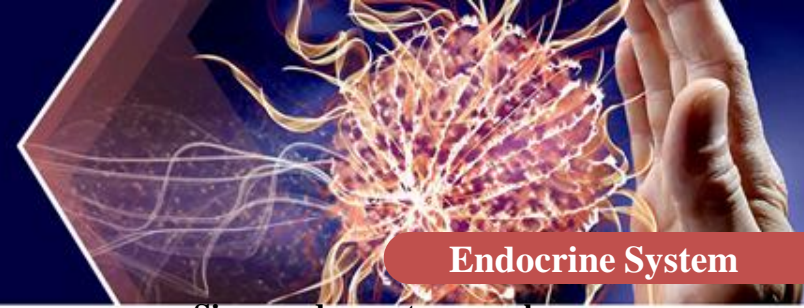
# ADVERSE EFFECTS OF IMMUNOTHERAPY

Mild flu like symptoms to inflammation of organs, autoimmune disorders and hypersensitivity reactions/ anaphylaxis



Body System	Toxicities
Dermatologic	Drug reaction with eosinophilia and systemic symptoms, Maculopapular rash, Psoriasis, Vitiligo
Gastrointestinal	Celiac disease, Enterocolitis, Gastritis, Pancreatitis
Endocrine	Adrenal insufficiency, Diabetes, Hypo/hyperthyroidism, Hypophysis
Renal	Granulomatous interstitial nephritis, Lupus-like GN
Cardiovascular	Cardiomyopathy, Myocarditis, Pericarditis
Pulmonary	Pleural effusion, Pneumonitis, Sarcoidosis
Nervous System	Aseptic meningitis, Encephalopathy, GBS, Myasthenia, Myelitis, Peripheral neuropathy
Hematologic	Hemolytic anemia, Thrombocytopenia, Neutropenia, Pancytopenia

# Immune related adverse events



## Respiratory Tract

### Signs and symptoms such as

- Dyspnea
- Cough

## Liver

### Signs such as

- Increased hepatic values (eg, AST, ALT or total bilirubin)

## Gastrointestinal Tract

### Signs and symptoms such as

- Diarrhea
- Stomach pain
- Blood in stool



## Endocrine System

### Signs and symptoms such as

- Psychological changes/mood swings
- Significant results for thyroid function tests and/or serum chemistry
- Fatigue
- Headache

## Kidneys

### Symptoms such as

- Blood in urine
- Increased serum creatinine
- Decreased urine output

## Skin

### Symptoms such as

- Itching
- Rash

< 1%: pancreatitis, uveitis, demyelination, autoimmune neuropathy (including facial nerve and abducens paralysis), Guillain-Barré-Syndrome, hypopituitarism and myasthenia syndrome.

# Considerations when managing immune-mediated adverse events



Early  
recognition of  
potential irAE



Close monitoring  
of signs/symptoms



Use of corticosteroids,  
withholding, or  
discontinuing therapy

**While some side effects of immunotherapy may appear similar to chemotherapy, they may need to be managed differently**

## 6. NURSES ROLE IN IMMUNOTHERAPY



# SAFE PREPRATION OF IMMUNOTHERAPY



- Prior to reconstitution of cytotoxic drugs ensure if the **patient's blood counts, electrolyte, liver and renal function test** values are within normal limits
- The order for the drug has to be **verified with the protocol**.
- The drug, diluents and the necessary disposable items should be placed in the **bio-safety cabinet**.
- After wearing the protective devices, reconstitute and dilute the drug following **strict aseptic techniques**.
- It is essential to label all the prepared bottles which are then to be **counter signed by the second person**.
- All potentially contaminated items (except sharps) are to be placed in the **disposable cover as per the institutional protocol**.





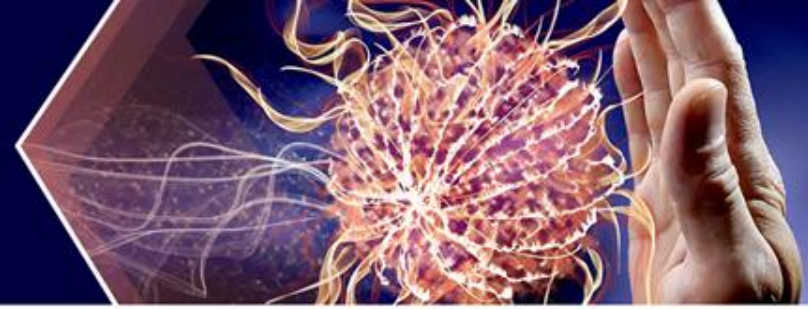
# SAFE ADMINISTRATION OF IMMUNOTHERAPY



- The procedure has s to be **explained** to the patient.
- The **hand hygiene policy** of the hospital is to be adhered to
- The **identity of the patient** is to be ensured by checking the name band of the patient and asking the patient to state his / her name.
- The **patency of the vein** for blood return is to be assessed using water for injection, sodium chloride or heparin saline. The drug is administered only when it is possible to aspirate and infuse fluid freely without pain or swelling.
- Drugs that have to be administered as continuous infusion are to be infused using an **infusion pump**.



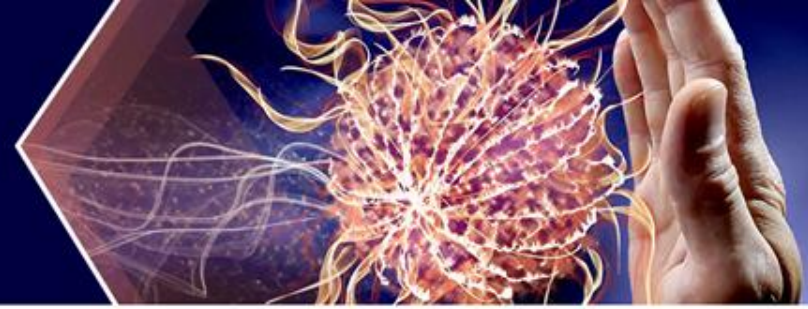
# Contd..



- The patient is to be advised to alert nursing staff in case of any **stinging, pain or discomfort**.
- Patients have to be observed for signs of **anaphylaxis** or any other adverse reaction.
- On completion of the infusion, the IV line is to **be flushed** with a compatible solution.
- The contaminated bottle and intravenous tubings are to be **disposed** as per protocol
- Hands have to be washed thoroughly after administration of drugs.
- The procedure has to be **documented** in the nurses record and should include:  
Pre-medication, sequence of drug administration, name of the drug dosage, route, diluent in which the drug is added, IV fluids infused and the rate of infusion, patient tolerance, any allergic reactions and educational interventions.



# Client and Family Teaching



- Minimize symptoms by managing fever and flulike symptoms: increase fluid intake, take analgesic and antipyretic medications and maintain bed rest until symptoms abate.
- Seek help for serious problems - dehydration from diarrhea/ hyper sensitivity
- Care for vascular access device /ambulatory pumps



# SUMMARY



- Thorough knowledge on immunotherapy
- Informed consent/Check baseline investigations
- Emergency kit / crash cart
- Monitoring the patient(checklist)
- Verification of order by senior physician
- Drug calculation and administration verification by a second registered nurse




- Pre medication



- Test dose



- Aseptic preparation & administration



- Disposal & documentation



- Prompt assessment and management of side effects/complications



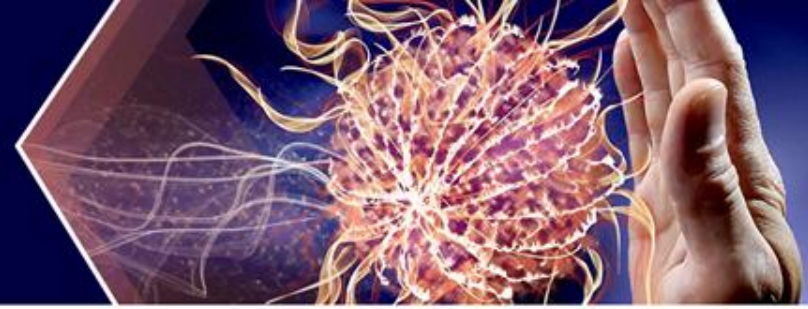
- Initiation of steroids



- Patient education

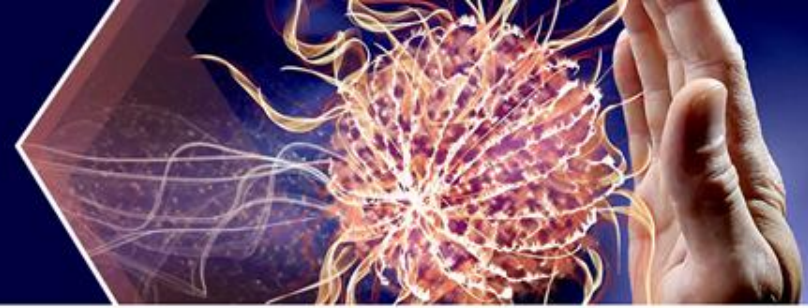


# Conclusion



- Immunotherapy is an established treatment method for multiple oncological diseases, spanning numerous solid tumours and haematological malignancies.
- The future of additional immunotherapeutic approaches is highly promising, as numerous cancer immunotherapies are currently in advanced phases of clinical development.
- Nurses have a challenging role to play in caring for patients with cancer immunotherapy

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*Thank  
You!*